IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

YUKSEL et al Atty. Ref.: **1577-164**

Serial No. **09/986,124** Group: **1617**

Filed: **November 7, 2001** Examiner: **WEBMAN, Edward J.**

For: **EXPANDABLE FOAM-LIKE BIOMATERIALS AND METHODS**

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May 24, 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPLICANTS' APPEAL BRIEF

Sir:

This Appeal is from the Examiner's rejection of claims 30-47, 53 and 54, all of the claims presently pending herein.[1] As will become evident from the following discussion, the Examiner's rejections are in error and, as such, reversal of the same is solicited.

I. Real Party In Interest

The real party in interest is the owner of the subject application, namely CryoLife, Inc.

II. Related Appeals and Interferences

There are no appeals and/or interferences pending related to the subject application.

[1] The claims on appeal appear in the Claims Appendix accompanying this Brief.

III. Status of Claims

A. The following claims are presently pending in this application and have been rejected in the Examiner's Official Action of April 8, 2005: Claims 30-47, 53 and 54.

B. The following claims have been cancelled during prosecution to date: Claims 1-20 and 48-52.

C. The following claims have been allowed: None

IV. Status of Amendments

No Amendments subsequent to the Official Action dated April 8, 2005 have been filed.

V. Summary of the Claimed Subject Matter

The present invention is directed toward kits comprising novel liquid, injectable, biomaterial that is transformed *in situ* to a foam-like, space filling, and adherent hydrogel. (page 2, lines 22-24) More specifically, the present invention is embodied in kits comprised of a two-part liquid system to achieve the *in situ* formation of a foam-like biomaterial. (page 2, lines 24-26) In some preferred embodiments, one of the components of the mixture may include a bicarbonate compound while the other component of the mixture may be provided with an acidic titrant in an amount sufficient to cause carbon dioxide gas to be evolved when the two components are mixed together. (page 5, line 24 through page 6, line 1)

According to independent claim 30, a kit for forming a solid cellular foam proteinaceous biopolymeric material comprises separate reactable aliquot portions consisting of a first aqueous solution containing a proteinaceous material, and a second aqueous solution which is reactable with the proteinaceous component of the first aqueous solution to form a solid proteinaceous biopolymeric material in response to

mixing of said first and second aqueous solutions. (page 4, lines 8-16) The first aqueous solution includes a blowing agent. (page 6, lines 5-15) The second aqueous solution includes an acidic titrant reactable on contact with the blowing agent sufficient to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while the proteinaceous material of the first aqueous solution reacts with the second aqueous solution to form the solid proteinaceous biopolymeric material. (page 6, line 25 through page 7, line 5)

According to independent claim 41, a kit for forming a solid cellular foam proteinaceous biopolymeric material comprises separate reactable aliquot portions consisting of a first aqueous solution containing bovine or human serum albumin, and a second aqueous solution containing a di- or polyaldehyde which is reactable with the bovine or human serum albumin of the first aqueous solution to form a solid proteinaceous biopolymeric material in response to mixing of said first and second aqueous solutions. (page 4, line 17 through page 5, line 6, and page 6, line 16-24) One of the first and second aqueous solutions includes a blowing agent. (page 5, lines 24-25) The other of the first and second aqueous solutions includes an acidic titrant reactable on contact with the blowing agent sufficient to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while the bovine or human serum albumin of said first aqueous solution reacts with said di- or polyaldehyde of said second aqueous solution to form said solid proteinaceous biopolymeric material. (page 5, line 25 through page 6, line 1 and page 6, line 25 through page 7, line 5)

VI. Issues to be Reviewed on Appeal

1. Does Nussinovitch (USP 6,589,328) anticipate claims 30 and 38 under 35 USC §102(e)?

2. Does the combination of Nussinovitch in view of Wang (USP 5,922,379) and Fattman et al (USP 6,326,524) render "obvious", and hence unpatentable, claims 30-47 and 53-54 under 35 USC §103(a)?

VII. Arguments

1. Claims 30 and 38 are not anticipated under 35 USC §102(e) by Nussinovitch[2]

It appears that the Examiner has not given any weight whatsoever to the fact that the first and second aqueous solutions according to the present invention are in fact ***separate*** from one another and that the first aqueous solution includes the proteinaceous material and one of a blowing agent or a titrant, while the second aqueous solution in accordance with the present invention comprises a component reactable with the proteinaceous material of the first solution and the other of the blowing agent or the titrant. Thus, ***concurrently*** with the reaction between the proteinaceous material of the first solution with the reactable component of the second solution ***in response to mixing*** of the two solutions, the blowing agent and titrant will likewise react to evolve a gas to impart a cellular foam structure to the otherwise solid proteinaceous biopolymeric material.

The Examiner's apparent misunderstanding of the present invention vis-à-vis Nussinovitch is exemplified by his comment that: "As to the claimed kit, the two solutions of Nussinovitch '328 constitute such."[3]

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[2] As the Board will note from the Evidence Appendix, a Rule 131 Declaration was submitted during prosecution so as to antedate the effective 102(e) date of Nussinovitch. However, the Examiner considered the Rule 131 Declaration to be insufficient for such purpose. See, Official Action dated October 26, 2004, at page 4, ¶1. Applicants are therefore accepting the viability of Nussinovitch as a reference against the claims pending herein. In any event, it will be noted that at least Example 1 of Nussinovitch is identical to its PCT counterpart from which it claims priority – i.e., PCT/EP/94/00107 – and which itself appears to be a viable reference also.

[3] Official Action dated April 8, 2005 at page 3, lines 16-17.

The "two solutions" of Nussinovitch do ***not*** however contain the components specifically required by the present applicants' independent claim 30. Specifically, applicants cannot discern any teaching in Nussinovitch whereby one of the "solutions" contains:

> "...an acidic titrant reactable on contact with the blowing agent sufficient to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while the proteinaceous material of the first aqueous solution reacts with the second aqueous solution to form the solid proteinaceous biopolymeric material."

It is true that, according to Nussinovitch, an alginate powder, calcium hydrogen orthophosphate and calcium carbonate are formed into an aqueous solution and then admixed with a solution of glucono-delta-lactone. However, this admixture is then:

> "...poured into a plastic container...and let to set there. After 48 hours, specimens were taken ***from the slab***."[4]

It is this "***slab***" – that is to say, solid material – that is then ***subsequently*** brought into contact with citric acid solution. Specifically, Nussinovitch discloses that the slab is "...immersed in citric acid solution 2%." (Column 5, line 40).

Hence, there is absolutely no disclosure that applicants can discern in Nussinovitch whereby one part of a two-part reactable solution kit contains both a proteinaceous material and a blowing agent, and wherein a second part of the two-part reactable solution kit comprises both a solution which is reactable with the proteinaceous material to form a biopolymeric material, and an acidic titrant reactable with the blowing agent sufficient to impart a cellular foam structure to thereto. Indeed, Nussinovitch's disclosure of ***first*** forming a solid material and ***then*** contacting the solid

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[4] See Nussinovitch at column 5, lines 37-38, emphasis added.

material after a considerable period of time cannot anticipate a kit as defined in claims 30 and 38 whereby ***two separate and distinct solutions***, when mixed are capable of forming in one simple step a cellular biopolymeric material.

To be sure, the explicit disclosure of Nussinovitch is that a ***solid non-cellular*** material is first formed which ***thereafter*** is brought into contact with citric acid to form a foam-like cellular structure. Thus, Nussinovitch cannot anticipate the present invention under 35 USC §102(e) since there is no disclosure therein of the two separate and distinct solutions containing the components as claimed herein and/or that the foam-like structure is achieved ***concurrently*** with the reaction of the proteinaceous material ***in response to*** mixing of the two aqueous solutions.

Directly contrary to the Examiner's assertions, therefore, Nussinovitch does not disclose the "solutions" as defined in the claims pending herein since nowhere does Nussinovitch suggest or disclose that the solutions may be merely mixed so as to achieve a reaction of the proteinaceous material to form a solid biopolymeric material ***concurrently*** while a blowing agent and a titrant react to simultaneously form a cellular structure therein. In other words, the present invention achieves a cellular biopolymeric material simultaneously during reaction whereas Nussinovitch teach first forming a solid non-cellular material followed by a treatment to render the same cellular. Nowhere does Nussinovitch teach or suggest that the therein disclosed material may be rendered cellular ***concurrently*** while a proteinaceous material is reacting to form a solid biopolymeric material.

Reversal of the rejection advanced under 35 USC §102(e) is therefore mandated.

2. Claims 30-47 and 53-54 are patentably unobvious under 35 USC §103(a) over Nussinovitch in view of Wang and Fattman et al.

The comments immediately above are equally germane to the issue of ***un***obviousness of the present invention as defined by independent claims 30 and 41,

and the claims dependent therefrom. Specifically, Nussinovitch's disclosure of first forming a solid material and then contacting the solid material after a considerable period of time teaches ***directly against*** the kits as defined in claims 30-47 and 53-54 whereby two separate and distinct solutions, when mixed are capable of forming in one simple step a cellular biopolymeric material.

The cited secondary references to both Wang and Fattman et al appear to be even less pertinent than Nussinovitch. Specifically, Wang merely teaches that a ***thermoplastic*** material may be made from protein, starch, cellulosic fiber and water. Fattman et al merely teaches that foams of hydrocolloids adhesives may be made. Neither Wang nor Fattman et al disclose or suggest a kit as claimed herein whereby one part of a two-part reactable solution kit contains both a proteinaceous material and a blowing agent, and wherein a second part of the two-part reactable solution kit comprises both a solution which is reactable with the proteinaceous material to form a biopolymeric material, and an acidic titrant reactable with the blowing agent sufficient to impart a cellular foam structure to thereto. Thus, neither Wang nor Fattman et al cure the deficiencies of Nussinovitch as discussed previously.

With respect to his rejection advanced under 35 USC §103(a), the Examiner has asserted that:

> "Applicants claim two solutions, then argue intended uses of those solutions. However, the references teach the claimed solutions. Intended uses are not considered patentable limitations in composition claims during prosecution before the USPTO."

With all due respect, applicants submit that the Examiner's assertions are both factually and legally erroneous.

Factually, it will be noted form the discussion above with respect to Nussinovitch, Wang and Fattman et al, that the references do ***not*** teach the claimed separate solutions which when mixed are capable of forming a cellular biopolymeric material *in situ*.

Legally, the applicants' claims and arguments are most certainly not directed to "intended uses" as asserted by the Examiner. Instead, the component parts of the presently claimed "kit" are directed to the physical and chemical attributes of the components in each of the separate solutions in the kit and to the interaction of such components when mixed to form the cellular biomaterial *in situ*.

This Board has explicitly recognized the propriety of claiming a kit of two chemical components that, ***when*** mixed form a phenol-formaldehyde resin foam. See, *Ex parte Sudan and Berchem*, 224 USPQ 614 (Bd. of Appeals 1983), *citing with approval In re Venezia*, 189 USPQ 189, 151 (CCPA 1976) ("[The claimed invention includes] present structural limitations on each part, which structural limitations are defined by how the parts are to be interconnected in the final assembly, if assembled.")

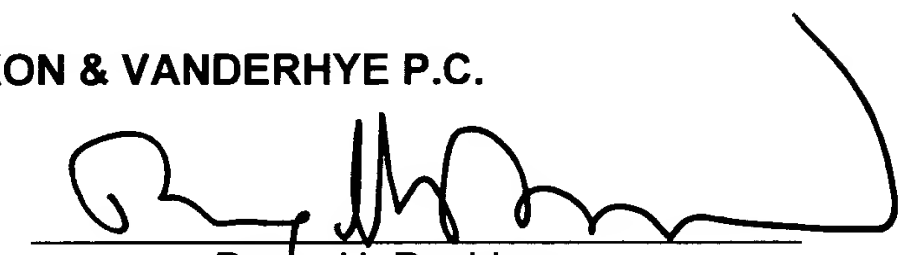
While *Ex parte Sudan and Berchem* dealt with the propriety of "kit" claims pursuant to 25 USC §112, second paragraph, the rationale expressed therein is relevant here. That is, what is claimed herein are components of a kit which recite definite physical and chemical attributes when such components interact....namely, that the components in the two separate solutions are reactable on contact to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while the proteinaceous material of the first aqueous solution reacts with the second aqueous solution to form the solid proteinaceous biopolymeric material. This interaction between the components of the presently claimed kit therefore is most certainly not merely an "intended use" as asserted by the Examiner, but instead are definite limitations of each component that must be given patentable weight.

The Examiner's rejection advanced under 35 USC §103(a) is therefore clearly based on reversible error since he has not given any patentable weight to the physical and chemical limitations attributed to the components of the two solutions defined in the claimed kit.

The Examiner's rejections of record are in error and must be reversed. Such favorable action is solicited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

Bryan H. Davidson
Reg. No. 30,251

BHD:maw
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

VII. CLAIMS APPENDIX

1-29. (canceled)

30. (previously presented) A kit for forming a solid cellular foam proteinaceous biopolymeric material comprising separate reactable aliquot portions consisting of a first aqueous solution containing a proteinaceous material, and a second aqueous solution which is reactable with the proteinaceous component of the first aqueous solution to form a solid proteinaceous biopolymeric material in response to mixing of said first and second aqueous solutions, wherein the first aqueous solution includes a blowing agent, and wherein said second aqueous solution includes an acidic titrant reactable on contact with the blowing agent sufficient to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while said proteinaceous material of said first aqueous solution reacts with said second aqueous solution to form said solid proteinaceous biopolymeric material.

31. (original) The kit of claim 30, wherein the first aqueous solution comprises human or animal-derived protein material and wherein the second aqueous solution comprises a di- or polyaldehyde.

32. (original) The kit of claim 31, wherein the protein is bovine or human serum albumin.

33. (original) The kit of claim 31, wherein the aldehyde is glutaraldehyde.

34. (original) The kit of any one of claims 30-33, wherein the inorganic blowing agent is a bicarbonate.

35. (original) The kit of claim 34, wherein the bicarbonate is at least one selected from the group consisting of bicarbonates of sodium, potassium, aluminum and iron.

36. (original) The kit of claim 30, wherein the blowing agent is an organic bicarbonate.

37. (previously presented) The kit of claim 30, wherein the blowing agent is ammonium bicarbonate.

38. (original) The kit of claim 30, wherein the acidic titrant is at least one acid selected from the group consisting of phosphoric acid, sulfuric acid, hydrochloric acid, acetic acid and citric acid.

39. (original) The kit of claim 30, wherein at least one of the first and second aqueous solutions includes biocompatible fibrous and/or particulate materials.

40. (original) The kit of claim 30, wherein the first and second aqueous solutions are sterilized.

41. (previously presented) A kit for forming a solid cellular foam proteinaceous biopolymeric material comprising separate reactable aliquot portions consisting of a first aqueous solution containing bovine or human serum albumin, and a second aqueous solution containing a di- or polyaldehyde which is reactable with the bovine or human serum albumin of the first aqueous solution to form a solid proteinaceous biopolymeric material in response to mixing of said first and second aqueous solutions, wherein one of the first and second aqueous solutions includes a blowing agent, and wherein the other of said first and second aqueous solutions includes an acidic titrant reactable on contact with the blowing agent sufficient to evolve a gas to impart a cellular foam structure to the proteinaceous biopolymeric material concurrently while said bovine or human serum albumin of said first aqueous solution reacts with said di- or polyaldehyde of said second aqueous solution to form said solid proteinaceous biopolymeric material.

42. (previously presented) The kit of claim 31, wherein the aldehyde is glutaraldehyde.

43. (previously presented) The kit of claim 41 or 42, wherein the inorganic blowing agent is a bicarbonate.

44. (previously presented) The kit of claim 43, wherein the bicarbonate is at least one selected from the group consisting of bicarbonates of sodium, potassium, aluminum and iron.

45. (previously presented) The kit of claim 41, wherein the blowing agent is an organic bicarbonate.

46. (previously presented) The kit of claim 41, wherein the blowing agent is ammonium bicarbonate.

47. (previously presented) The kit of claim 41, wherein the acidic titrant is at least one acid selected from the group consisting of phosphoric acid, sulfuric acid, hydrochloric acid, acetic acid and citric acid.

48 – 52 (cancelled)

53. (previously presented) The kit of claim 41, wherein at least one of the first and second aqueous solutions includes biocompatible fibrous and/or particulate materials.

54. (previously presented) The kit of claim 41, wherein the first and second aqueous solutions are sterilized.

IX. EVIDENCE APPENDIX

Evidence Description	Statement re Record Entry
"Declaration Under Rule 131" – Evidence of claimed invention being made in this country prior to June 18, 1997	Submitted concurrently as a part of and entered into the record with the Amendment dated July 7, 2004.

X. RELATED PROCEEDINGS APPENDIX

(Not Applicable)

XI. Certificate of Service

(Not Applicable)